Invited State-Of-The-Art Review

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Biomimetics and planetary health – a review of human diseases in interaction with the environment and ecosystem

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ABSTRACT

Elderly people and patients with chronic lifestyle diseases are at risk of being hit harder by environmental influences. Environmental impacts increase the risk of various lifestyle diseases. Biomimetics gives us a unique opportunity to find new treatments for lifestyle diseases and counteract health effects of environmental threats. A biomimetic alliance for better health achieved through cross-disciplinal collaboration may not only contribute to better health but also to a better and more sustainable environment: What is good for the planet is good for our health.

KEY POINTS

- Planetary health embraces the concept that human welfare depends on the well-being of ecological systems.
- One consequence of environmental stressors has been the stimulation of inflammatory and oxidative stress pathways that promote lifestyle diseases and accelerated ageing.
- Biomimicry aims to mimic ingenious solutions that have evolved in nature for different applications that benefit humans.
- Learning from nature provide opportunities for management and solutions to environmental challenges.

Recent changes to the natural systems of the planet are of such enormous magnitude that the geological period we live in has been given its own name - the Anthropocene. The expansive and uncontrolled behaviour of Homo sapiens, i.e. the "wise man", has brought considerable environmental problems such as global warming, deforestation, loss of natural habitats for animals, pollution of air, water and soil, and lack of clean water. The global temperature has risen by 1.16 °C since 1880 and continues to increase at a faster rate, which increases the risk of extreme weather conditions [1]. The summer of 2023 will be remembered as “the summer of temperature records and wildfires”. Despite these warning signs, emissions continue at an even faster rate. The rate at which temperatures are rising has challenged our ability to adapt our lifestyles to a fossil-free society. In a scenario with persistently high CO_2 emissions, a collapse of biological diversity in tropical oceans will occur before the year 2030 and spread to tropical forests before 2050 [2]. Tropical forests are now approaching a critical temperature threshold that could affect photosynthesis [3]. Thus, we need to change our current lifestyle, radically reduce CO_2 emissions and protect biodiversity.

WE ARE WITNESSING A NEW DISEASE PANORAMA

Global health is also challenged by an aging population and epidemics of lifestyle diseases characterised by “inflammaging" and a downregulated expression of nuclear factor erythroid 2-related factor 2 (Nrf2) [4]. This ancient cytoprotective transcription factor counteracts inflammation and oxidative stress by upregulating hundreds of cytoprotective genes [4]. It evolved around 530 million years ago as animals and plants began to explore the world above the oceans and were exposed to oxygen after the great oxygenation event [5]. The increase in incidence of lifestyle diseases in Anthropocene is partly due to genetic, epigenetic and functional adaptations that have occurred during evolution as a result of changes during human development due to changes in climate, food availability and pandemics [6]. Planetary health is a new research discipline that integrates studies of human health with environmental and animal health changes [7].

We have already seen tangible evidence of how disturbances in the global environment affect human health. In Central America, and other warm parts of the world, epidemics of chronic kidney disease (CKD) are reported in young males working in the sugarcane fields in a hot climate [8]. As physical work in heat appears to cause the disease, the problem is expected to increase with warmer temperatures. In Brazil, more than 7% of all hospitalisations for kidney disease are caused by high temperatures **[9]**. Even assuming the most favourable scenario, climate change will increase the risk of cardiovascular disease (CVD) [10]. When the temperature rises above > 29 °C, the risk of dying from CVD increases and heat waves increase the risk for CVD through a combination of dehydration, inflammation, disturbed salt balance, rapid pulse, increased oxygen consumption and impaired vascular reactivity [11]. Many Nepalese guest workers aged 25-35 years died of CVD while working in hot conditions to prepare for the Soccer World Cup in Qatar [12] – some of them returned home with CKD [13].

Since the infamous fog in the Meuse Valley in Belgium in 1930 and smog in London in 1952, it has been evident that air pollution causes disease and death. Epidemiological studies have shown connections between air pollution and a risk of life-style diseases such as CKD [14], obesity, type-2 diabetes [15] and CVD [16]. Air pollution is also associated with accelerated cognitive decline and increased risk of Alzheimer's disease [17]. Women exposed to air pollution are twice as likely to develop dementia [18], and 17-20% of all cases of CKD in low- and middle-income countries is linked to air pollution [19]. The connection between lack of clean water and increased morbidity has been evident for hundreds of years [20]. Lack of clean water and global warming cause chronic dehydration, which may increase the risk of type-2 diabetes [21] and obesity [22]. The association between heat and obesity may in part be explained by activation of the fructose and vasopressin systems [23]. Global warming also has other negative effects on our health, such as a more sedentary lifestyle, an increased intake of high-calorie drinks and impaired mitochondrial function with increased oxidative stress – established risk factors for lifestyle diseases [24].

BIOMIMETICS HELP US FIND NEW HEALTH SOLUTIONS

Due to the current serious environmental situation, humans are challenged more than never before and we must urgently find new and innovative solutions. The enormous diversity of about 8.7 million species is one of the most striking aspects of life on our planet. Since animal life arose about 650 million years ago, animals have survived or not based on whether their adaptations to environmental change and the previous five mass extinctions have been effective. Species that failed to adapt to changed circumstances became extinct. Because humans overexploited and destroyed ecosystems over the past century, it will take millions of years for the planet to recover from this loss of biodiversity [25]. This will have a catastrophic effect because the concept of biodiversity does not only include the number of existing species on the planet but also the sum of the unique evolutionary development that occurred over millions of years for each species [25].

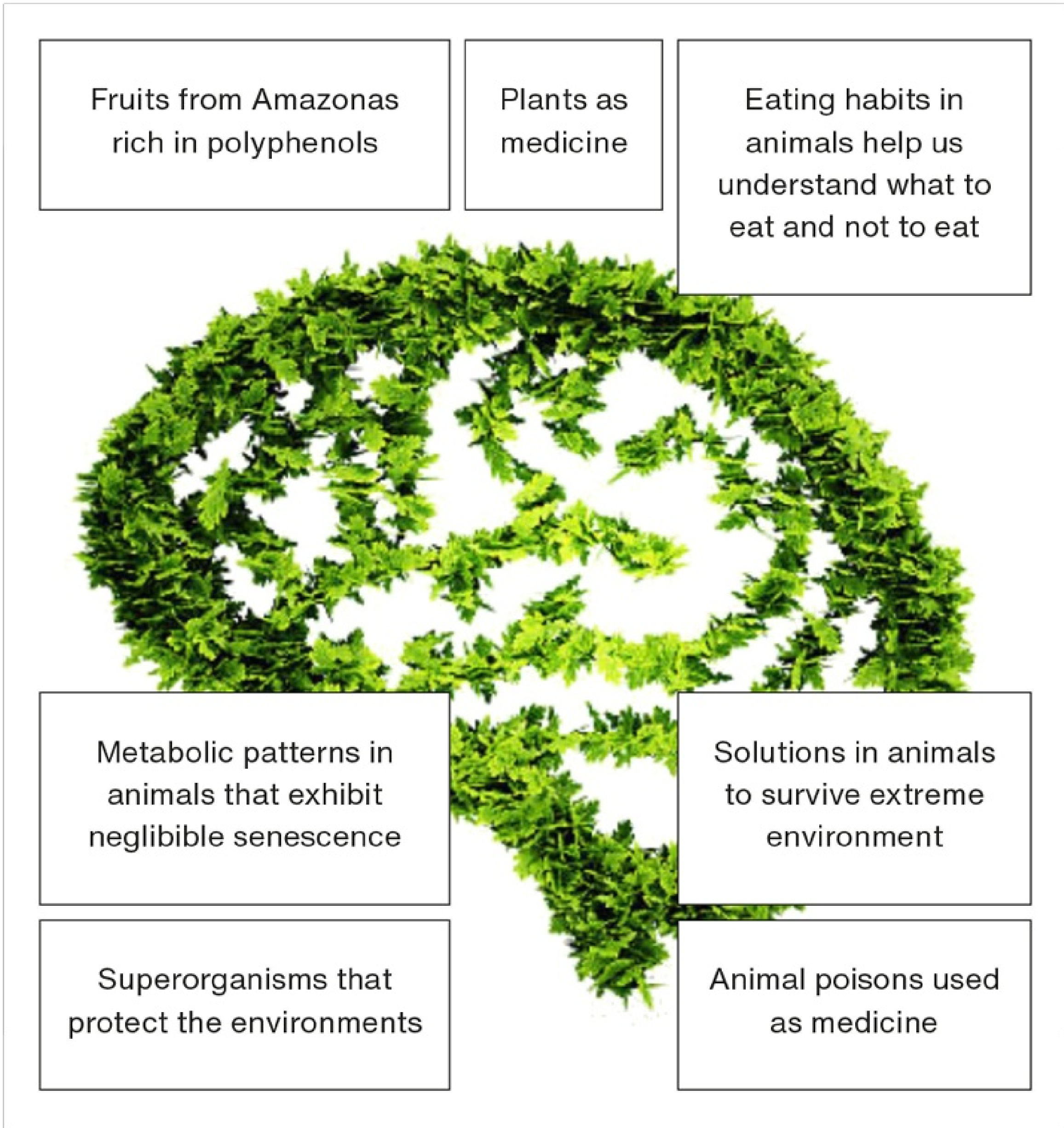
Instead of exploiting and destroying the natural balance, we should learn from and emulate the ingenious natural solutions that have evolved over time. We may adopt a biomimetic approach and base our decision on a biomimetic rather than the current antropocenic organisational approach [26]. Although innovation-based opportunities based on solutions in nature have proven successful in a wide range of fields, biomimetics has yet to develop its full potential in biomedical science [27]. A biomimetic approach using the intelligence of nature may complement current biological approaches that largely focus on research in mice and rats conducted in unnatural laboratory environments [28]. Since nature is never careless or cheats in its evolutionary experiments, the risk that biomimetic research leads to incorrect results is minor.

SOLUTIONS FOR LIFESTYLE DISEASES AND ENVRIONMENTAL THREATS ALREADY EXIST IN NATURE

The literature is full of examples where humans have learned from wild animals that developed ingenious solutions that protect them against chronic lifestyle diseases [28]. Hibernating bears do not develop insulin resistance or type-2 diabetes despite pronounced obesity during the fall [29]. Furthermore, despite months of anuria, inactivity and reduced kidney function during hibernation, bears do not suffer from osteoporosis, inflammation or muscle wasting [30]. During hibernation, bears undergo natural immunisation against atherosclerosis [31] and have developed ingenious mechanisms for thrombo-protection [32]. However, when bears are deprived of their normal habits and environment, they undergo accelerated ageing [33]. The link between fat accumulation and water balance in long-term water-deprived species, such as camels and blue whales, provide clues about metabolic survival mechanisms that have been lost in modern society with a sedentary lifestyle and overconsumption of high-caloric foods and drinks [34].

Other animals have developed unique mechanisms for protection against high blood pressure (giraffes), organ regeneration (sharks, lizards and spiders), cancer protection (elephants and naked mole rats), blood sugar control (the Gila lizard), protection against UV light (hippopotamus) and acute kidney failure (deep-diving seals) that should inspire researchers to find new solutions for lifestyle diseases [28]. Some animals employ anti-aging mechanisms, such as the naked mole rat, Icelandic clam and the Greenland shark, including mechanisms that may potentially be used to arrest ageing-related diseases [35]. Rockfish are of interest since their life span may vary from 30-40 years to more than 200 years. Thus, sets of genes found across rockfish may help to explain differences in longevity. As genes associated with flavonoid metabolism affected ageing, this fish may teach us to eat more vegetables and fruits [36]. Nature counteracts exaggerations from within and bats, bears, seals, and long-lived naked mole rats have an upregulated Nrf2 system likely to protect them in exceptional habitats [4]. It has also been reported that Nrf2 agonists protect animals against air pollution [37] and heat stress [38]. The intelligence of nature may be used to improve human health (**Figure 1**).

FIGURE 1 Examples of solutions that nature's intelligence can provide for the benefit of human health and climate.



We may also learn from animals that show an increased vulnerability to a specific disease. One example is felines (cats, tigers, and lions), which show a greatly increased risk of CKD [39, 40]. Although several causes may explain the increased risk of CKD in felines, findings in cats reinforce epidemiological studies showing that increased intake of red and especially ultra-processed meat increases the risk of CKD [41, 42]. Increased consumption of red meat also has health implications in humans [43]. Mounting evidence shows that ultra-processed food increases the risk for type-2 diabetes, obesity, CVD, dementia, fatty liver and CKD [44]. Moreover, a large study from the UK showed a connection between ultra-processed food and cancer [45]. A higher consumption of ultra-processed food is also associated with shorter telomeres and higher biological age [46]. Additionally, ultra-processed food is addictive [47] and has negative environmental effects [48]. As food that is good for health is also good for the climate, a radical transformation of the food system is urgently needed [49].

LOSS OF BIODIVERSITY REDUCES OUR CHANCES TO DISCOVER NEW DRUGS

One of the best examples to date of a successful biomimetic application is the development of the antihypertensive drug captopril from the venomous Brazilian viper. Its effect on the renin-angiotensin system has been a game changer for patients with CKD, diabetes and CVD. A more recent example of a drug developed from nature is the venom of the Gila lizard, which is one of three venomous lizards in the world. After years of development, research into the lizard's venom has produced a new and effective treatment for type-2 diabetes and weight loss [50].

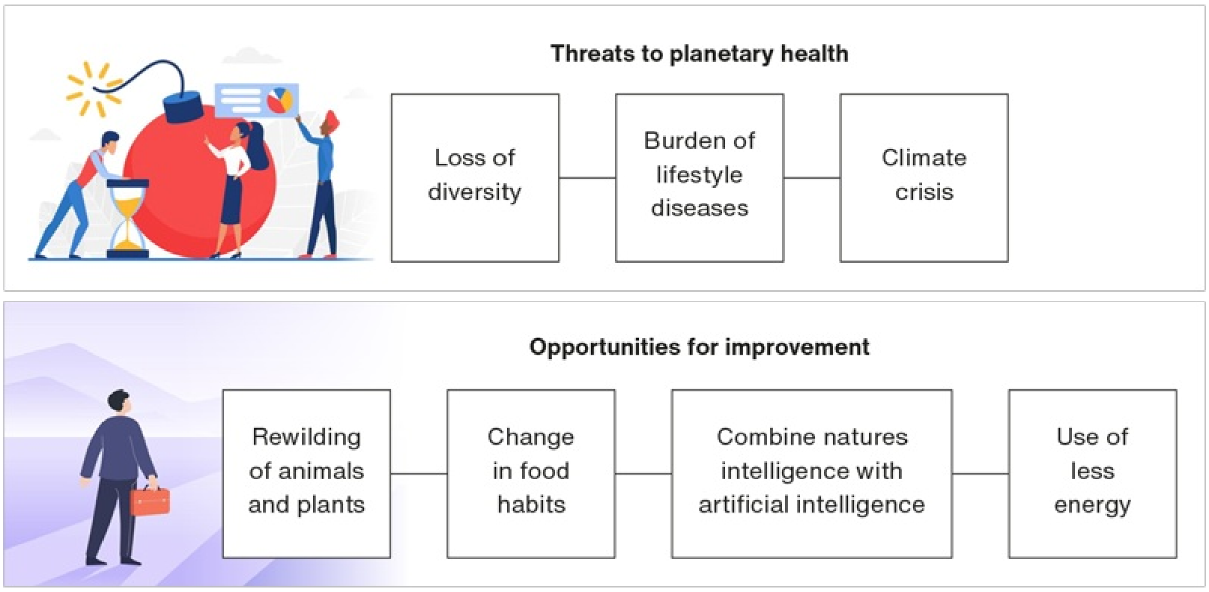
Since approximately one third of the medications used in healthcare originate from nature, the development of future medicines depends on preserved diversity. With more than 50,000 species of plants, it is of the outmost importance that deforestation of the Amazon is prevented, not only for environmental but also for health reasons. Unfortunately, the loss of different habitats and ecosystems means that we are missing out on a unique opportunity to identify biomimetic solutions for human diseases. It is possible to stimulate the cytoprotective transcription factor Nrf2 with substances from the plant kingdom such as sulforaphane. This offers an alternative route to evidence-based non-pharmacological treatments to improve health according to the concept of food as medicine [51]. Treatment with broccoli sprouts rich in sulforaphane is as effective as metformin in difficult-to-regulate type-2 diabetes [52]. It is ironic that - just as we are beginning to gain evidence that tailored nutritional therapy may influence lifestyle diseases - this development is threatened by a disturbed external environment of global warming, air pollution and deforestation.

BIOMIMETIC ALLIANCE TO IMPROVE PLANETARY HEALTH

Due to the current dire situation, humans are challenged like never before and we must find new solutions. Many people are waiting for a new wave of innovations based on a sustainability revolution with ingenious new solutions that may reduce man's environmental and climate footprint. Artificial intelligence (AI) may have an important complementary ability in relation to difficult decisions. It may also assist us and ensure that the data are interpreted objectively and that the right decision is made more quickly. However, AI is not harmless and needs careful control. If we are to rely solely on our own abilities and AI, several prerequisites for solving multiple problems on our planet are missing. We need to cover the patches where our own human intelligence and AI are insufficient. Here, nature with its long-term perspective, reuse, adaptation, diversity and self-healing ability may contribute with solutions that have been developed slowly but methodically over millions of years.

We need to adopt a strategy for the entire health of the planet in which studies of human health are integrated with studies of the environment and animal health. To better prevent and treat lifestyle diseases that increase with age, we can learn from nature. By adopting a biomimetic approach, we should be able to learn from the ingenious solutions that have evolved in nature to better meet the environmental threats we are currently facing. Detailed studies of survival mechanisms developed in animals can identify mechanisms of importance for prevention and treatment of human lifestyle diseases and effects of environmental influences. This approach requires multidisciplinary collaboration between doctors, veterinarians, climate scientists, ecologists, and biologists [28]. It is in the squabbles and clashes between different disciplines that we will most likely make important discoveries. If we are to adopt a biomimetic approach to research, immediate action is required as a rapid loss of species diversity and habitats may limit this opportunity to learn from nature (**Figure 2**). As the shortcomings of Homo sapiens may be remedied by the strengths of AI and the intelligence nature, this is an opportunity we should not miss. Although humans are good problem solvers, we need immediate help. Nature is still there to assist but cannot wait much longer.

FIGURE 2 Threats to planetary health and opportunities for improvement.



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